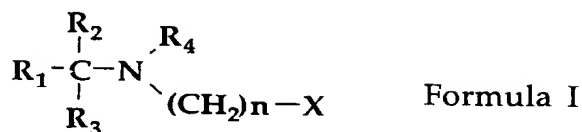


WE CLAIM:

1. A compound of the Formula I



- 5 wherein:

$\text{R}_1$  is  $(\text{CH}_2)_m\text{CH}_3$  where  $m$  is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to 17 carbon atoms,

$\text{R}_2 = \text{H}, \text{CH}_3$  or  $\text{CH}_2\text{CH}_3$ ,

- 10  $\text{R}_3 = \text{H}$  or  $\text{CH}_3$ ,

$\text{R}_4 = \text{H}$  or  $\text{CH}_3$ ,

$\text{R}_5 =$  lower alkyl having from 1 to 5 carbon atoms,

$n$  is an integer in the range from 1 to 3,

- 15 and  $\text{X}$  is carboxyl ( $\text{COOH}$ ) or carbalkoxy ( $\text{COOR}_5$ ), cyano ( $\text{C}\equiv\text{N}$ ), phosphonic acid ( $\text{PO}_3\text{H}_2$ ), phosphonate ester ( $\text{PO}_3[\text{R}_5]_2$ ) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.

2. A compound of the Formula I according to claim 1 wherein:

$\text{R}_1 = (\text{CH}_2)_m\text{CH}_3$  where  $m$  is 0 or an integer in the range from 1 to 16,

$\text{R}_2 = \text{CH}_3$ ,

- 20  $\text{R}_3 = \text{H}$ ,

$\text{R}_4 = \text{H}$  or  $\text{CH}_3$ ,

$\text{R}_5 =$  lower alkyl having from 1 to 5 carbon atoms,

$n$  is an integer in the range from 1 to 3,

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and X is carboxyl (COOH) or carbalkoxy (COOR<sub>5</sub>), cyano (C≡N), phosphonic acid (PO<sub>3</sub>H<sub>2</sub>), phosphonate ester (PO<sub>3</sub>[R<sub>5</sub>]<sub>2</sub>) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.

3. A compound of the Formula I according to claim 1 wherein:

5 R<sub>1</sub> = (CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub> where m is 0 or an integer in the range from 1 to 16,

R<sub>2</sub> = CH<sub>3</sub>,

R<sub>3</sub> = H,

R<sub>4</sub> = H or CH<sub>3</sub>,

R<sub>5</sub> = lower alkyl having from 1 to 5 carbon atoms,

10 n is an integer in the range from 1 to 3,

and X is carboxyl (COOH) or carbalkoxy (COOR<sub>5</sub>) cyano (C≡N), phosphonic acid (PO<sub>3</sub>H<sub>2</sub>), phosphonate ester (PO<sub>3</sub>[R<sub>5</sub>]<sub>2</sub>) or 5-tetrazole, as a substantially pure enantiomer in the R-configuration, or a pharmaceutically acceptable salt thereof.

15 4. A compound of the formula I according to claim 1 wherein:

R<sub>1</sub> = (CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub> where m is 0 or an integer in the range from 1 to 16,

R<sub>2</sub> = CH<sub>3</sub>,

R<sub>3</sub> = H,

R<sub>4</sub> = H or CH<sub>3</sub>,

20 R<sub>5</sub> = lower alkyl having from 1 to 5 carbon atoms,

n is an integer in the range from 1 to 3,

and X is carboxyl (COOH) or carbalkoxy (COOR<sub>5</sub>) cyano (C≡N), phosphonic acid (PO<sub>3</sub>H<sub>2</sub>), phosphonate ester (PO<sub>3</sub>[R<sub>5</sub>]<sub>2</sub>) or 5-tetrazole, as a substantially pure enantiomer in the S-configuration, or a pharmaceutically acceptable salt thereof.

25

5. A compound of the Formula I according to claim 1 wherein:

R<sub>1</sub> = (CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub> where m is 0 or an integer in the range from 1 to 16,

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 $R_2 = \text{CH}_3$ , $R_3 = \text{H}$ , $R_4 = \text{H}$  or  $\text{CH}_3$ , $R_5 =$  lower alkyl having from 1 to 5 carbon atoms,5  $n$  is an integer in the range from 1 to 3,

and  $X$  is carboxyl ( $\text{COOH}$ ) or carbalkoxy ( $\text{COOR}_5$ ), cyano ( $\text{C}\equiv\text{N}$ ), phosphonic acid ( $\text{PO}_3\text{H}_2$ ), phosphonate ester ( $\text{PO}_3[\text{R}_5]_2$ ) or 5-tetrazole, wherein the compound is racemic or achiral and with the following exclusions:

a) for  $X = \text{COOH}$ ;  $n = 1$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:10  $R_2 = \text{H}$  and  $m = 1$  to 4, 6, 7, 9, 11, or 13, and $R_2 = \text{CH}_3$  and  $m = 0, 1$  or 2;b) for  $X = \text{COOH}$ ;  $n = 1$ ;  $R_3 = \text{H}$ ;  $R_4 = \text{CH}_3$ , exclude compounds for which: $R_2 = \text{H}$  and  $m = 2$  or 3, and $R_2 = \text{CH}_3$  and  $m = 0$ ;15 c) for  $X = \text{COOR}_5$ ;  $n = 1$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which: $R_2 = \text{H}$  and  $m = 1$  to 4, or 9, and $R_2 = \text{CH}_3$  and  $m = 0$  or 1, and $R_5 =$  methyl, ethyl, t-butyl;d) for  $X = \text{COOH}$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:20  $R_2 = \text{H}$  and  $m = 1$  to 4, 6, 9 or 11, and $R_2 = \text{CH}_3$  and  $m = 0, 1$  or 4;e) for  $X = \text{COOH}$ ;  $n = 2$ ;  $R_3 = \text{H}$ ;  $R_4 = \text{CH}_3$ , exclude compounds for which: $R_2 = \text{H}$  and  $m = 1$  or 2;f) for  $X = \text{COOR}_5$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:25  $R_2 = \text{H}$  and  $m = 1$  to 5, 9 or 15, $R_2 = \text{CH}_3$  and  $m = 0$  or 1, and $R_5 =$  methyl, ethyl, t-butyl;g) for  $X = \text{COOR}_5$ ;  $n = 2$ ;  $R_3 = \text{H}$ ;  $R_4 = \text{CH}_3$ , exclude compounds for which: $R_2 = \text{H}$  and  $m = 1$  or 2,30  $R_2 = \text{CH}_3$  and  $m = 0$ , and

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$R_5$  = methyl, ethyl, t-butyl;

h) for  $X = \text{COOH}$ ;  $n = 3$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

$R_2 = \text{H}$  and  $m = 2$  or  $6$ ;

i) for  $X = \text{COOR}_5$ ;  $n = 3$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

5  $R_2 = \text{H}$  and  $m = 2$ ,

$R_2 = \text{CH}_3$  and  $m = 0$  or  $1$ , and

$R_5$  = methyl, ethyl, t-butyl;

j) for  $X = \text{C}\equiv\text{N}$  (cyano);  $n = 1$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

10  $R_2 = \text{H}$  and  $m = 1, 2, 4, 5$  or  $6$ , and

$R_2 = \text{CH}_3$  and  $m = 0, 1$  or  $2$ ;

k) for  $X = \text{C}\equiv\text{N}$ ;  $n = 1$ ;  $R_3 = \text{H}$ ;  $R_4 = \text{CH}_3$ , exclude compounds for which:

$R_2 = \text{H}$  and  $m = 1$ , and

$R_2 = \text{CH}_3$  and  $m = 0$ ;

15 l) for  $X = \text{C}\equiv\text{N}$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

$R_2 = \text{H}$  and  $m = 1, 2, 3, 4$  or  $6$ , and

$R_2 = \text{CH}_3$  and  $m = 0, 1$  or  $4$ ;

m) for  $X = \text{C}\equiv\text{N}$ ;  $n = 2$ ;  $R_3 = \text{H}$ ;  $R_4 = \text{CH}_3$ , exclude compounds for which:

$R_2 = \text{H}$  and  $m = 2$ , and

20  $R_2 = \text{CH}_3$  and  $m = 0$ ;

n) for  $X = \text{C}\equiv\text{N}$ ;  $n = 3$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

$R_2 = \text{H}$  and  $m = 1$  to  $4$ , and

$R_2 = \text{CH}_3$  and  $m = 1$  or  $2$ ;

o) for  $X = \text{PO}_3\text{H}_2$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

25  $R_2 = \text{CH}_3$  and  $m = 0, 1$  or  $5$ ;

p) for  $X = \text{PO}_3(\text{R}_5)_2$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

$R_2 = \text{CH}_3$  and  $m = 0$  or  $1$ , and

$R_5$  = ethyl; and

q) for  $X = 5\text{-tetrazole}$ ;  $n = 2$ ;  $R_3 = R_4 = \text{H}$ , exclude compounds for which:

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 $R_2 = CH_3$  and  $m = 0$ .

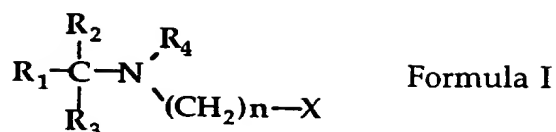
6. A compound of the Formula I according to any one of claims 1 to 5 wherein  $R_1$  is substituted with at least one of the substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide, sulfone, phenyl, halogen-substituted phenyl, hydroxy-substituted phenyl, cycloalkyl having from 3 to 6 carbon atoms and heterocyclic substituents having between 3 and 6 atoms, of which from 1 to 3 are heteroatoms selected from O, S and/or N.
7. A compound according to claim 3, wherein said compound of formula I is selected from the group consisting of:
- (R)-3-(2-Heptylamino)propionic acid;
  - (R)-3-(2-Heptylmethylamino)propionic acid;
  - Methyl (R)-3-(2-heptylamino)propionate;
  - Methyl (R)-3-(2-heptylmethylamino)propionate;
  - (R)-2-(2-Pentylamino)acetonitrile;
  - (R)-2-(2-Pentylmethylamino)acetonitrile;
  - (R)-3-(2-Heptylamino)propionitrile;
  - (R)-3-(2-Heptylmethylamino)propionitrile;
  - (R)-2-(2-Pentylamino)ethanephosphonic acid;
  - (R)-2-(2-Pentylmethylamino)ethanephosphonic acid; and
  - (R)-2-(2-Heptylamino)ethane-5-tetrazole.
8. A compound according to claim 4, wherein said compound of formula I is selected from the group consisting of:
- (S)-2-(2-Heptylamino)acetic acid;
  - (S)-2-(2-Heptylmethylamino)acetic acid;
  - Methyl (S)-2-(2-heptylamino)acetate;
  - Methyl (S)-2-(2-heptylmethylamino)acetate;
  - (S)-2-(2-Heptylamino)acetonitrile;
  - (S)-2-(2-Heptylmethylamino)acetonitrile;

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(S)-2-(2-Heptylamino)ethanephosphonic acid; and  
(S)-2-(2-Heptylmethylamino)ethanephosphonic acid.

9. A compound according to claim 5, wherein said compound of formula I is selected from the group consisting of:
- 5 2-(1-Hexylmethylamino)acetic acid;  
3-(2-Propylmethylamino)propionic acid;  
Methyl 2-(2-propylmethylamino)acetate;  
Methyl 2-(1-hexylmethylamino)acetate;  
Methyl 3-(1-hexylmethylamino)propionate;
- 10 2-(1-Hexylamino)acetonitrile;  
2-(1-Hexylmethylamino)acetonitrile;  
3-(3-Pentylamino)propionitrile;  
3-(3-Pentylmethylamino)propionitrile;  
2-(2-Propylamino)ethanephosphonic acid; and
- 15 2-(2-Propylmethylamino)ethanephosphonic acid.
10. A compound according to any one of claims 1 to 9 in the form of a hydrochloride salt.
11. A compound according to any one of claims 3 to 9 wherein m is an integer from 1 to 12.
- 20 12. A compound according to any one of claims 3 to 9 wherein m is an integer from 1 to 9.
13. A composition for the treatment or prevention of a disease in which cell death occurs by apoptosis, which composition comprises an effective amount of a compound having the formula I:

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wherein:

- 5  $\text{R}_1$  is  $(\text{CH}_2)_m\text{CH}_3$  where  $m$  is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to 17 carbon atoms,
- $\text{R}_2 = \text{H}, \text{CH}_3$  or  $\text{CH}_2\text{CH}_3$ ,
- $\text{R}_3 = \text{H}$  or  $\text{CH}_3$ ,
- $\text{R}_4 = \text{H}$  or  $\text{CH}_3$
- 10  $\text{R}_5 =$  lower alkyl having from 1 to 5 carbon atoms,
- $n$  is an integer in the range from 1 to 3,
- and  $\text{X}$  is carboxyl ( $\text{COOH}$ ), carbalkoxy ( $\text{COOR}_5$ ), cyano ( $\text{C}\equiv\text{N}$ ), phosphonic acid ( $\text{PO}_3\text{H}_2$ ), phosphonate ester ( $\text{PO}_3[\text{R}_5]_2$ ) or 5-tetrazole, or a pharmaceutically acceptable salt thereof, in admixture with a suitable
- 15 diluent or carrier.

14. A composition according to claim 13, wherein:

- $\text{R}_1$  is  $(\text{CH}_2)_m\text{CH}_3$  where  $m$  is 0 or an integer in the range from 1 to 16,
- $\text{R}_2 = \text{CH}_3$ ,
- $\text{R}_3 = \text{H}$ ,
- 20  $\text{R}_4 = \text{H}$  or  $\text{CH}_3$ ,
- $\text{R}_5 =$  lower alkyl having from 1 to 5 carbon atoms,
- $n$  is an integer in the range from 1 to 3,
- and  $\text{X}$  is carboxyl ( $\text{COOH}$ ), carbalkoxy ( $\text{COOR}_5$ ), cyano ( $\text{C}\equiv\text{N}$ ), phosphonic acid ( $\text{PO}_3\text{H}_2$ ), phosphonate ester ( $\text{PO}_3[\text{R}_5]_2$ ) or 5-tetrazole, or a
- 25 pharmaceutically acceptable salt thereof, in admixture with a suitable diluent or carrier.

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15. A composition according to claim 13 or 14, wherein  $R_1$  differs from  $R_2$ ,  $R_3 = H$  and the compound is in the R-configuration.

16. A composition according to claim 13 or 14, wherein  $R_1$  differs from  $R_2$ ,  $R_3 = H$  and the compound is in the S-configuration.

5 17. A composition according to any one of claims 13 to 16, wherein  $R_1$  is substituted with at least one of the substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide, sulfone, phenyl, halogen-substituted phenyl, hydroxy-substituted phenyl, cycloalkyl having  
10 and 6 carbon atoms and heterocyclic substituents having between 3 and 6 atoms, of which from 1 to 3 are heteroatoms selected from O, S and/or N.

18. A composition according to claim 13 or 14, wherein said compound of formula I is selected from the group consisting of:

2-(2-Propylamino)acetic acid;

15 2-(1-Hexylamino)acetic acid;

(S)-2-(2-Heptylamino)acetic acid;

3-(2-Propylamino)propionic acid;

3-(1-Hexylamino)propionic acid;

(R)-3-(2-Heptylamino)propionic acid;

20 2-(2-Propylmethylamino)acetic acid;

2-(1-Hexylmethylamino)acetic acid;

(S)-2-(2-Heptylmethylamino)acetic acid;

3-(2-Propylmethylamino)propionic acid;

3-(1-Hexylmethylamino)propionic acid;

25 (R)-3-(2-Heptylmethylamino)propionic acid;

2-(2-Propylamino)acetonitrile;

(R)-2-(2-Pentylamino)acetonitrile;

2-(1-Hexylamino)acetonitrile;

(S)-2-(2-Heptylamino)acetonitrile;

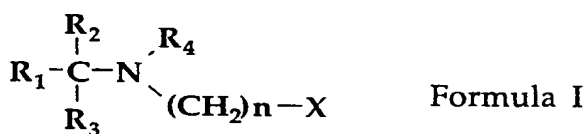


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- (R)-3-(2-Heptylamino)propionitrile;  
 2-(2-Propylmethylamino)acetonitrile;  
 (R)-2-(2-Pentylmethylamino)acetonitrile;  
 2-(1-Hexylmethylamino)acetonitrile;  
 5 (S)-2-(2-Heptylmethylamino)acetonitrile;  
 (R)-3-(2-Heptylmethylamino)propionitrile;  
 2-(2-Propylamino)ethanephosphonic acid;  
 (R)-2-(2-Pentylamino)ethanephosphonic acid;  
 (S)-2-(2-Heptylamino)ethanephosphonic acid;  
 10 2-(2-Propylmethylamino)ethanephosphonic acid;  
 (S)-2-(2-Heptylmethylamino)ethanephosphonic acid; and  
 (R)-2-(2-Heptylamino)ethane-5-tetrazole.

19. A composition according to claim 18, wherein the compound of formula I is in the form of a hydrochloride salt.

- 15 20. A use of a compound of the formula I for the treatment or prevention of a disease in which cell death occurs by apoptosis, wherein said compound has the formula I:



20 wherein:

R<sub>1</sub> is (CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub> where m is 0 or an integer in the range from 1 to 16, or an alkenyl, alkynyl, alkoxy, alkylthio, or alkyl sulfinyl group having from 2 to 17 carbon atoms,

R<sub>2</sub> = H, CH<sub>3</sub> or CH<sub>2</sub>CH<sub>3</sub>

25 R<sub>3</sub> = H or CH<sub>3</sub>

R<sub>4</sub> = H or CH<sub>3</sub>

R<sub>5</sub> = lower alkyl having 1 to 5 carbon atoms

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n is an integer in the range from 1 to 3,  
and X is carboxyl (COOH), carbalkoxy (COOR<sub>5</sub>), cyano (C≡N), phosphonic acid (PO<sub>3</sub>H<sub>2</sub>), phosphonate ester (PO<sub>3</sub>[R<sub>5</sub>]<sub>2</sub>) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.

- 5     21.            A use according to claim 20, wherein  
R<sub>1</sub> is (CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub> where m is 0 or an integer in the range from 1 to 16,  
R<sub>2</sub> = CH<sub>3</sub>,  
R<sub>3</sub> = H,  
R<sub>4</sub> = H or CH<sub>3</sub>,  
10    R<sub>5</sub> = lower alkyl having 1 to 5 carbon atoms,  
n is an integer in the range from 1 to 3,  
and X is carboxyl (COOH), carbalkoxy (COOR<sub>5</sub>), cyano (C≡N), phosphonic acid (PO<sub>3</sub>H<sub>2</sub>), phosphonate ester (PO<sub>3</sub>[R<sub>5</sub>]<sub>2</sub>) or 5-tetrazole, or a pharmaceutically acceptable salt thereof.
- 15    22.            A use according to claim 20 or 21 wherein R<sub>1</sub> is substituted with at least one of the substituents selected from hydroxy, aldehyde, oxo, lower acyloxy, halogen, thio, sulfoxide, sulfone, phenyl, halogen-substituted phenyl, hydroxy-substituted phenyl, cycloalkyl having from 3 to 6 carbon atoms and heterocyclic substituents having between 3 and 6 atoms, of which  
20    from 1 to 3 are heteroatoms selected from O, S and/or N.
23.            A use according to claim 20 wherein said compound of Formula I is selected from the group consisting of:  
2-(2-Propylamino)acetic acid;  
2-(1-Hexylamino)acetic acid;  
25    (S)-2-(2-Heptylamino)acetic acid;  
3-(2-Propylamino)propionic acid;  
3-(1-Hexylamino)propionic acid;  
(R)-3-(2-Heptylamino)propionic acid;

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- 2-(2-Propylmethylamino)acetic acid;  
2-(1-Hexylmethylamino)acetic acid;  
(S)-2-(2-Heptylmethylamino)acetic acid;  
3-(2-Propylmethylamino)propionic acid;  
5 3-(1-Hexylmethylamino)propionic acid;  
(R)-3-(2-Heptylmethylamino)propionic acid;  
2-(2-Propylamino)acetonitrile;  
(R)-2-(2-Pentylamino)acetonitrile;  
2-(1-Hexylamino)acetonitrile;  
10 (S)-2-(2-Heptylamino)acetonitrile;  
(R)-3-(2-Heptylamino)propionitrile;  
2-(2-Propylmethylamino)acetonitrile;  
(R)-2-(2-Pentylmethylamino)acetonitrile;  
2-(1-Hexylmethylamino)acetonitrile;  
15 (S)-2-(2-Heptylmethylamino)acetonitrile;  
(R)-3-(2-Heptylmethylamino)propionitrile;  
2-(2-Propylamino)ethanephosphonic acid;  
(R)-2-(2-Pentylamino)ethanephosphonic acid;  
(S)-2-(2-Heptylamino)ethanephosphonic acid;  
20 2-(2-Propylmethylamino)ethanephosphonic acid;  
(S)-2-(2-Heptylmethylamino)ethanephosphonic acid; and  
(R)-2-(2-Heptylamino)ethane-5-tetrazole.

24. A use according to any one of claims 20 to 23 wherein the  
disease is selected from the group consisting of stroke, head trauma, Bell's  
25 palsy, spinal cord injury, Alzheimer's disease, Parkinson's disease, Pick's  
disease, amyotrophic lateral sclerosis, Huntington's disease, multiple  
sclerosis, cardiac myopathies, nephropathy, retinopathy, diabetic  
complications, glaucoma and idiopathic neuropathies.

25. A use according to any one of claims 20 to 24, for the treatment  
30 of a human.

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26. A commercial package for the treatment or prevention of a disease in which cell death occurs by apoptosis, said package comprising a pharmaceutical composition according to any one of claims 13 to 19, together with instructions for use in the treatment or prevention of diseases
- 5 in which cell death occurs by apoptosis.